

We Claim:

1. A method of producing monoclonal antibodies specific to an antigen of low immunogenicity comprising:
 - a. conjugating the antigen chemically to a carrier molecule;
 - 5 b. immunizing an animal with the conjugated antigen;
 - c. harvesting B cells from the animal;
 - d. creating a hybridoma from the harvested B cells;
 - e. screening the hybridomas for specificity to the native antigen.
2. The method of claim 1, wherein the carrier molecule is HSP70.
- 10 3. The method of claim 1, wherein the animal has an intact immune system.
4. The method of claim 1, wherein the animal is a mammal.
5. The method of claim 1, wherein the B cells are harvested from ascites.
6. The method of claim 1, wherein the B cells are harvested from lymph nodes.
7. The method of claim 1, wherein the B cells are harvested from blood.
- 15 8. The method of claim 1, wherein the B cells are harvested from spleen.
9. The method of claim 1, wherein the hybridoma is created using an immortal mouse cell.
10. The method of claim 9, wherein the immortal mouse cell is a mouse myeloma cell.
11. The method of claim 1, wherein the hybridoma is created using an immortal human
- 20 cell.
12. The method of claim 1, wherein the hybridoma is created using an immortal rat cell.
13. The method of claim 1, wherein the screening for specificity is done by a method chosen from the group consisting of radioimmunoassay, enzyme-linked immunosorbant assay, "sandwich" immunoassay, immunoradiometric assay, gel
- 25 diffusion precipitation reaction, immunodiffusion assay, *in situ* immunoassay, western blot, precipitation reaction, agglutination assay, complement fixation assay, immunofluorescence assay, protein A assay, virus visualization assay, biological activity modulation assay, and immunoelectrophoresis assay.
14. A composition comprising a monoclonal antibody specific to an antigen of low
- 30 immunogenicity produced by:
 - a. conjugating the antigen chemically to a carrier molecule;
 - b. immunizing an animal with the conjugated antigen;
 - c. harvesting B cells from the animal;
 - d. creating a hybridoma from the harvested B cells; and
 - 35 e. screening the hybridomas for specificity to the native antigen.

15. The composition of claim 14, wherein the carrier molecule is HSP70.
16. The composition of claim 14, wherein the animal has an intact immune system
17. The composition of claim 14, wherein the animal is a mammal.
18. The composition of claim 14, wherein the B cells are harvested from ascites.
- 5 19. The composition of claim 14, wherein the B cells are harvested from lymph nodes.
20. The composition of claim 14, wherein the B cells are harvested from blood.
21. The composition of claim 14, wherein the B cells are harvested from spleen.
22. The composition of claim 14, wherein the hybridoma is created using mouse myeloma cells.
- 10 23. The composition of claim 14, wherein the hybridoma is created using an immortal human cell.
24. The composition of claim 14, wherein the hybridoma is created using an immortal rat cell.
25. The composition of claim 14, wherein the screening for specificity is done by a method
15 chosen from the group consisting of radioimmunoassay, enzyme-linked immunosorbant assay, "sandwich" immunoassay, immunoradiometric assay, gel diffusion precipitation reaction, immunodiffusion assay, *in situ* immunoassay, western blot, precipitation reaction, agglutination assay, complement fixation assay, immunofluorescence assay, protein A assay, virus visualization assay, biological
20 activity modulation assay, and immunoelectrophoresis assay.
26. A method of producing monoclonal antibodies specific to E7 oncoprotein comprising:
a. conjugating the E7 oncoprotein chemically to a carrier molecule;
b. immunizing an animal with the conjugated antigen;
c. harvesting B cells from the animal;
25 d. creating a hybridoma from the harvested B cells; and
e. screening the hybridomas for specificity to the native E7 oncoprotein.
27. The method of claim 26, wherein the chemical conjugation comprises:
a. creating a plasmid with a nucleotide sequence encoding E7 oncoprotein and a nucleotide sequence encoding HSP70; and
30 b. transfecting a host cell with the plasmid, wherein the host cell transcribes the nucleotide sequences into the conjugated E7 oncoprotein.
28. The method of claim 27, wherein the nucleotide sequence encoding E7 oncoprotein is SEQ ID NO: 1.
29. The method of claim 27, wherein the nucleotide sequence encoding E7 oncoprotein is
35 SEQ ID NO: 3.

30. The method of claim 27, wherein the nucleotide sequence encoding HSP70 is SEQ ID NO: 5.
31. The method of claim of claim 27, wherein the host cell is *E. coli*.
32. The method of claim 26, wherein the carrier molecule is HSP70.
- 5 33. The method of claim 26, wherein the animal has an intact immune system
34. The method of claim 26, wherein the animal is a mammal.
35. The method claim 34, wherein the animal is a mouse.
36. The method of claim 26, wherein the B cells are harvested from ascites.
37. The method of claim 26, wherein the B cells are harvested from lymph nodes.
- 10 38. The method of claim 26, wherein the B cells are harvested from blood.
39. The method of claim 26, wherein the B cells are harvested from spleen.
40. The method of claim 26, wherein the hybridoma is created using an immortal mouse cell.
41. The method of claim 40, wherein the immortal mouse cell is a mouse myeloma cell.
- 15 42. The mouse myeloma cell of claim 41 is an Sp2/0-Ag14 myeloma cell.
43. The method of claim 26, wherein the hybridoma is created using an immortal human cell.
44. The method of claim 26, wherein the hybridoma is created using an immortal rat cell.
45. The method of claim 26, wherein the screening for specificity is done by a method
- 20 chosen from the group consisting of radioimmunoassay, enzyme-linked immunosorbant assay, "sandwich" immunoassay, immunoradiometric assay, gel diffusion precipitation reaction, immunodiffusion assay, *in situ* immunoassay, western blot, precipitation reaction, agglutination assay, complement fixation assay, immunofluorescence assay, protein A assay, virus visualization assay, biological
- 25 activity modulation assay, and immunoelectrophoresis assay.
46. A composition comprising monoclonal antibodies specific to E7 oncoprotein produced by a method comprising:
- a. conjugating the E7 oncoprotein chemically to a carrier molecule;
- b. immunizing an animal with the conjugated antigen;
- 30 c. harvesting B cells from the animal;
- d. creating a hybridoma from the harvested B cells; and
- e. screening the hybridomas for specificity to the native E7 oncoprotein.
47. The composition of claim 46, wherein the chemical conjugation comprises:
- a. creating a plasmid with an nucleotide sequence encoding E7 oncoprotein and an
- 35 nucleotide sequence encoding HSP70; and

- b. transfecting a host cell with the plasmid, wherein the host cell transcribes the nucleotide sequences into the conjugated E7 oncoprotein.
48. The composition of claim 47, wherein the nucleotide sequence encoding E7 oncoprotein is SEQ ID NO: 1.
- 5 49. The composition of claim 47, wherein the nucleotide sequence encoding E7 oncoprotein is SEQ ID NO: 3.
50. The composition of claim 47, wherein the nucleotide sequence encoding HSP70 is SEQ ID NO: 5.
51. The composition of claim 47, wherein the host cell is *E. coli*.
- 10 52. The composition of claim 46, wherein the carrier molecule is HSP70.
53. The composition of claim 46, wherein the animal has an intact immune system
54. The composition of claim 46, wherein the animal is a mammal.
55. The composition claim 54, wherein the animal is a mouse.
56. The composition of claim 46, wherein the B cells are harvested from ascites.
- 15 57. The composition of claim 46, wherein the B cells are harvested from lymph nodes.
58. The composition of claim 46, wherein the B cells are harvested from blood.
59. The composition of claim 46, wherein the B cells are harvested from spleen.
60. The composition of claim 46, wherein the hybridoma is created using an immortal mouse cell.
- 20 61. The composition of claim 60, wherein the immortal mouse cell is a mouse myeloma cell.
62. The mouse myeloma cell of claim 61 is an Sp2/0-Ag14 myeloma cell.
63. The composition of claim 46, wherein the hybridoma is created using an immortal human cell.
- 25 64. The composition of claim 46, wherein the hybridoma is created using an immortal rat cell.
65. The composition of claim 46, wherein the screening for specificity is done by a method chosen from the group consisting of radioimmunoassay, enzyme-linked immunosorbant assay, "sandwich" immunoassay, immunoradiometric assay, gel
- 30 diffusion precipitation reaction, immunodiffusion assay, *in situ* immunoassay, western blot, precipitation reaction, agglutination assay, complement fixation assay, immunofluorescence assay, protein A assay, virus visualization assay, biological activity modulation assay, and immunoelectrophoresis assay.
66. A method of using monoclonal antibodies specific to E7 oncoprotein for the detection
- 35 of cervical intraepithelial neoplasia comprising:

- a. obtaining a specimen of cervical epithelial cells; and
 - b. screening the specimen for the presence of E7 oncoprotein.
67. The method of claim 66, wherein the screening method for the presence of E7 oncoprotein is chosen from the group consisting of radioimmunoassay, enzyme-linked immunosorbant assay, "sandwich" immunoassay, immunoradiometric assay, gel diffusion precipitation reaction, immunodiffusion assay, *in situ* immunoassay, western blot, precipitation reaction, agglutination assay, complement fixation assay, immunofluorescence assay, protein A assay, virus visualization assay, biological activity modulation assay, and immunoelectrophoresis assay.
68. The method of claim 66, wherein the presence of E7 oncoprotein is equal to or greater than 0.05 ng/ml.
69. The method claim 66, wherein the monoclonal antibodies comprise of at least two immunoglobulin isotypes.
70. The monoclonal antibodies of claim 69, wherein one immunoglobulin isotype is IgG2a.
71. The monoclonal antibodies of claim 69, wherein one immunoglobulin isotype is IgG2b.
72. The monoclonal antibodies of claim 69, wherein one immunoglobulin isotype has specificity for a different antigenic determinant than the second immunoglobulin isotype.
73. A kit for determining if a subject is at risk for developing cervical intraepithelial neoplasia comprising:
- a. at least one reagent that specifically detects E7 oncoprotein; and
 - b. instructions for determining that the subject is at increased risk of developing cervical intraepithelial neoplasia.
74. The reagent of claim 73 is the monoclonal antibodies of claim 46.
75. A method of producing monoclonal antibodies specific to a Prion protein peptide comprising:
- a. conjugating the Prion protein peptide chemically to a carrier molecule;
 - b. immunizing an animal with the conjugated antigen;
 - c. harvesting B cells from the animal;
 - d. creating a hybridoma from the harvested B cells; and
 - e. screening the hybridomas for specificity to the native Prion protein.
76. The method of claim 75, wherein the conjugating is performed chemically using glutaraldehyde.

77. The method of claim 75, wherein the Prion protein peptide is SEQ ID NO: 6.
78. The method of claim 75, wherein the Prion protein peptide is SEQ ID NO: 7.
79. The method of claim 75, wherein the Prion protein peptide is SEQ ID NO: 9.
80. The method of claim 75, wherein the carrier molecule is HSP70.
- 5 81. The method of claim 75, wherein the animal is a mouse.
82. The method of claim 75, wherein the screening is done using an enzyme-linked immunosorbent assay.
83. A kit for for determining if a subject is at risk for developing spongiform encephalopathy comprising:
- 10 a. at least one reagent that specifically detects Prion protein; and
- b. instructions for determining that the subject is at increased risk of developing spongiform encephalopathy.
84. A method of producing monoclonal antibodies specific to hyaluronic acid comprising:
- 15 a. conjugating the hyaluronic acid chemically to a carrier molecule;
- b. immunizing an animal with the conjugated antigen;
- c. harvesting B cells from the animal;
- d. creating a hybridoma from the harvested B cells; and
- e. screening the hybridomas for specificity to the native hyaluronic acid.
85. A method of producing monoclonal antibodies specific to matrix metalloprotease 3 comprising:
- 20 a. conjugating the matrix metalloprotease 3 chemically to a carrier molecule;
- b. immunizing an animal with the conjugated antigen;
- c. harvesting B cells from the animal;
- d. creating a hybridoma from the harvested B cells; and
- 25 e. screening the hybridomas for specificity to the native matrix metalloprotease 3.
86. The method of claim 85, wherein the conjugating is performed chemically using glutaraldehyde.
87. The method of claim 85, wherein the carrier molecule is HSP70.
88. The method of claim 85, wherein the animal is a mouse.
- 30 89. The method of claim 85, wherein the screening is done using an enzyme-linked immunosorbent assay.